



ELSEVIER

CASE REPORT

JOURNAL of  
CARDIOLOGY

Official Journal of the Japanese College of Cardiology

www.elsevier.com/locate/jjcc

# Novel neointimal formation over sirolimus-eluting stents identified by coronary angioscopy and optical coherence tomography

Daisuke Murakami (MD)<sup>a</sup>, Masamichi Takano (MD)<sup>b,\*</sup>,  
Masanori Yamamoto (MD)<sup>a</sup>, Shigenobu Inami (MD)<sup>a</sup>,  
Takayoshi Ohba (MD)<sup>a</sup>, Yoshihiko Seino (MD, FJCC)<sup>a</sup>,  
Kyoichi Mizuno (MD, FJCC)<sup>b</sup>

<sup>a</sup> Cardiovascular Center, Chiba-Hokusoh Hospital, Nippon Medical School, Chiba, Japan

<sup>b</sup> Division of Cardiology, Nippon Medical School, 1-1-5 Sendagi, Bunkyo-ku, Tokyo 113-8602, Japan

Received 10 July 2008; received in revised form 7 August 2008; accepted 14 August 2008

Available online 17 October 2008

## KEYWORDS

Angioscopy;  
Coronary artery disease;  
Optical coherence  
tomography;  
Stent

**Summary** Neointimal proliferation after sirolimus-eluting stent (SES) implantation is generally inhibited by the pharmacological effects of sirolimus in comparison to bare metal stent (BMS). Neointimal hyperplasia after BMS implantation is mainly composed of vascular smooth muscle cells, and is usually observed as a white mass by angioscopy and as a layer of uniform signal intensity without attenuation on optical coherence tomography (OCT). In this case, angioscopic color of the neointima covering the SES was obviously yellow and OCT signal patterns of the neointima showed rapid attenuation similar to lipid tissues in atherosclerotic lesions. These findings suggest that neointima within the SES is quite different from that of the BMS and may contain atherosclerotic components.

© 2008 Japanese College of Cardiology. Published by Elsevier Ireland Ltd. All rights reserved.

## Introduction

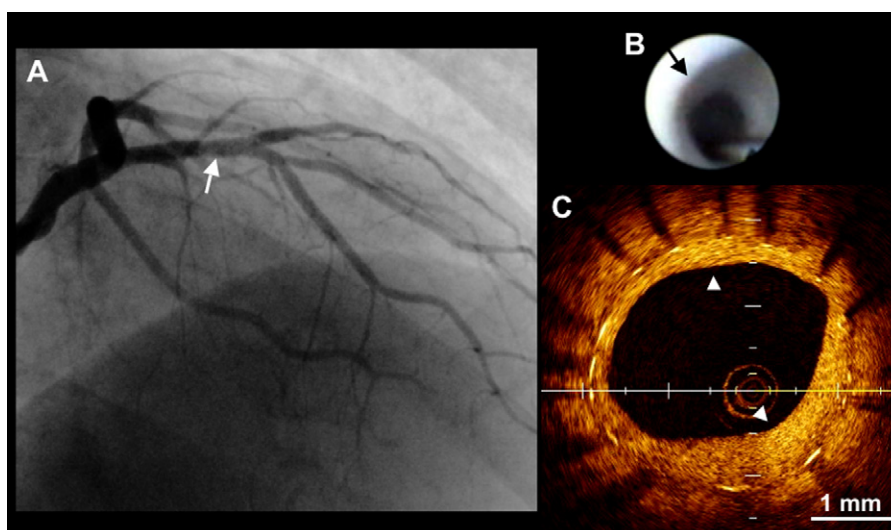
Although neointimal growth inside the stent is seen as angiographic lumen loss, information on the neointimal characteristics is not available from coronary angiograms. Angioscopy provides direct

visualization of the lumen and macroscopic diagnosis for intravascular structures. Optical coherence tomography (OCT) is also capable of tissue characterization on the basis of its signal patterns [1,2]. Neointimal hyperplasia, recognized as a white mass by angioscopy and as a rather thick layer of uniform signals without their attenuation by OCT [3,4], covers fully over the bare metal stent (BMS) within several months following its implantation (Fig. 1).

\* Corresponding author. Tel.: +81 3 3822 2131;

fax: +81 3 5685 0987.

E-mail address: [takanom@nms.ac.jp](mailto:takanom@nms.ac.jp) (M. Takano).

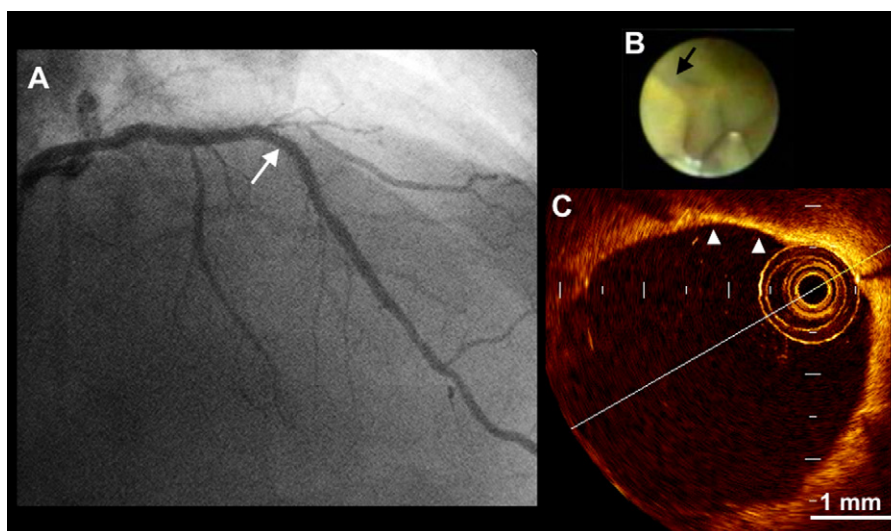


**Figure 1** Typical findings of angiography, and optical coherence tomography after bare metal stent (BMS) implantation. (A) A 43-year-old man with stable angina pectoris received implantation of a BMS (3.5 mm  $\times$  13 mm) in the left anterior descending artery. Six-month follow-up angiogram shows no in-stent restenosis (arrow). (B) Angioscopy shows white neointima covers completely over the BMS (arrow) and the struts are invisible. (C) Circumferential stent struts with strong signals are identified by cross-sectional image of optical coherence tomography. Neointima inside the struts has uniform signals without their attenuation (arrowheads).

## Case report

A 64-year-old man with stable angina pectoris underwent successful percutaneous coronary intervention. Three overlapping sirolimus-eluting stents (SESs) (3.5 mm  $\times$  18 mm, 3.5 mm  $\times$  23 mm, and 3.0 mm  $\times$  23 mm) were deployed for a diffuse

long lesion in the left anterior descending artery. No in-stent restenosis within the SES segment was found on 6-month follow-up angiograms. Coronary angioscopy showed localized yellow neointima covered over the struts of the SES in the proximal overlapping segment. OCT images demonstrated that thin membrane inside the struts of this



**Figure 2** Novel findings of angiography and optical coherence tomography after sirolimus-eluting stents (SESs) implantation. (A) Three SESs were deployed in the left anterior descending artery. Six-month follow-up angiogram shows no in-stent restenosis (arrows). (B) Angioscopy shows yellow neointima covers over the SES (arrow), whereas some of the struts are uncovered in the proximal overlapping segment. (C) In this overlapping segment, thin membranous structure inside the struts of inner stent is partially recognized by optical coherence tomography. Neointima has strong signals with their rapid attenuation similar to a lipid plaque (arrowheads). Although struts of inner stent are clearly seen, those of outer stent are not visible owing to backscattering of the neointima.

segment had high signal spots on the surface accompanying their rapid attenuation (Fig. 2).

## Discussion

Although there are several reports on the progress in neointimal coverage after SES implantation [3–5], characteristics of the neointima have been little known. In the present case, appearance of the neointima over the SES was quite different from usual neointima inside the conventional BMS. The neointima had yellow color on the basis of angioscopic observation. Despite the fact that our OCT image quality was inadequate for circumferential evaluation of the coronary lumen because of non-centered image wire position [6], OCT pattern of the neointima clearly showed superficially strong signals with backscattering. According to established criteria for the coronary plaques based on angioscopic and OCT findings [1,2], characteristics of the neointima were consistent with a lipid tissue. Previous pathological examinations revealed that drug-eluting stent implantation-induced inflammatory responses, such as infiltration of several kinds of inflammatory cells, giant cells, T-lymphocytes, neutrophils, and macrophages around the struts [7–9]. Infiltrated macrophages in lipid-rich plaques in vivo are identified as high signal spots by OCT like this case [10]. The novel neointimal proliferation was found locally in the overlapping SES segment in this case. The expression of tissue factors included in advanced atherosclerotic plaques is enhanced by sirolimus [7,11]. In the overlapping segment, therefore, double layers of polymer and/or drug may evoke excessive inflammation and expression of tissue factors as an experimental study indicated [8]. To date, atherosclerosis is considered to be an inflammatory disease [12]. These inflammatory responses invited by SES may promote atherosclerotic changes of the tissue around stent struts including neointima. There is no pathological confirmation that lipid-like neointima based on the characteristics of intracoronary imaging devices actually contains lipid tissue, because the neointima is extremely thin and is unworthy of receiving directional coronary atherectomy. Although the precise mechanisms of appearance of the novel neointima are uncertain, the above inflammatory or atherosclerotic changes provoked by SES may

affect the lipid-like neointima similar to atherosclerotic tissues. Our angioscopic and OCT images indicate that atherosclerotic process in the neointimal hyperplasia inside the SES may differ from that of the BMS.

## References

- [1] Yabushita H, Bouma BE, Houser SL, Aretz HT, Jang IK, Schlendorf KH, et al. Characterization of human atherosclerosis by optical coherence tomography. *Circulation* 2002;106:1640–5.
- [2] Takano M, Jang IK, Inami S, Yamamoto M, Murakami D, Okamatsu K, et al. In-vivo comparison of optical coherence tomography and angiography for the evaluation of coronary plaque characteristics. *Am J Cardiol* 2008;101:471–6.
- [3] Takano M, Ohba T, Inami S, Seimiya K, Sakai S, Mizuno K. Angioscopic differences in neointimal coverage and in persistence of thrombus between sirolimus-eluting stents and bare metal stents after a 6-months implantation. *Eur Heart J* 2006;27:2189–95.
- [4] Xie Y, Takano M, Murakami D, Yamamoto M, Okamatsu K, Inami S, et al. Comparison of neointimal coverage by optical coherence tomography of a sirolimus-eluting stent versus a bare metal stent three months after implantation. *Am J Cardiol* 2008;102:27–31.
- [5] Takano M, Yamamoto M, Inami S, Murakami D, Seimiya K, Ohba T, et al. Long-term follow-up evaluation after sirolimus-eluting stent implantation by optical coherence tomography: do uncovered struts persist? *J Am Coll Cardiol* 2008;51:968–9.
- [6] Asawa K, Kataoka T, Kobayashi Y, Hasegawa T, Nishioka H, Yamashita H, et al. Method analysis for optimal continuous imaging using intravascular ultrasound optical coherence tomography. *J Cardiol* 2006;47:133–41.
- [7] Luscher TF, Steffel J, Eberli FR, Joner M, Nakazawa G, Tanner FC, et al. Drug-eluting stent and coronary thrombosis: biological mechanisms and clinical implications. *Circulation* 2007;115:1051–8.
- [8] Finn AV, Kolodgie FD, Harnek J, Guerrero LJ, Acampado E, Tefera K, et al. Differential response of delayed healing and persistent inflammation at sites of overlapping sirolimus- or paclitaxel-eluting stents. *Circulation* 2005;112:270–8.
- [9] Virmani R, Liistro F, Stankovic G, Di Mario C, Montorfano M, Farb A, et al. Mechanism of late in-stent restenosis after implantation of a paclitaxel derivate-eluting polymer stent system in human. *Circulation* 2002;106:2649–51.
- [10] MacNeill BD, Jang IK, Bouma BE, Iftimia N, Takano M, Yabushita H, et al. Focal and multi-focal plaque macrophage distributions in patients with acute and stable presentations of coronary artery disease. *J Am Coll Cardiol* 2004;44:972–9.
- [11] Fuster V, Moreno PR, Fayad ZA, Corti R, Badimon JJ. Atherothrombosis and high-risk plaque. Part I. Evolving concept. *J Am Coll Cardiol* 2005;46:937–54.
- [12] Ross R. Atherosclerosis—an inflammatory disease. *N Engl J Med* 1999;340:115–26.

